REMARKS

In the office action, the specification and claims have been objected to, and the claims have been rejected under 35 USC §§ 101, 112, 102 and 103. In response, Applicants have amended the specification, cancelled claims 1-13, added new claims 14-22, and provide the herein remarks. Accordingly, claims 14-22 are pending in the application. Reconsideration is respectfully requested.

Specification

The Examiner has requested that the use of the term "Superdex" in the specification be capitalized because it is a trademark. In response, Applicants have amended the application to capitalize SUPERDEX.

Claim Objections

The claims have been objected to on several grounds. Claims 1, 4, 8, 9, 11, and 13 have been objected to due to syntax. Claims 10 and 11 have been objected to as being substantial duplicates of claims 6 and 7, respectively. Claim 2 has been objected to for allegedly failing to further limit the subject matter of a previous claim.

In response, Applicants have cancelled the claims and submitted new claims. The new claims recite proper syntax, avoid being duplicative and are proper dependant claims. Accordingly, Applicants submit that the above objections have been rendered moot.

Rejection Under §101

In the office action, claims 8-12 have been rejected under 35 USC §101 as being directed to non-statutory subject matter. In particular, the Examiner contends that the claims lack required steps.

In response, Applicants have cancelled claims 8-12 and added new claims 14-22. New claims 14-22 recite steps where appropriate. Accordingly, Applicants respectfully submit that the rejection under §101 has been rendered moot.

Rejections Under §112, First Paragraph

Claims 1-13 have been rejected under 35 USC §112, first paragraph, as allegedly lacking enablement for use in humans as a vaccine. The Examiner contends that the claims are excessively broad because they read on treating "any IL-15 expression related disease." The Examiner notes that there are allegedly no examples showing use of the claimed vaccine capable of treating any disease in humans.

The Examiner does recognize that the specification provides examples of use of the claimed composition to induce an immune response in monkeys which results in the production of neutralizing IL-15 antibodies. However, the Examiner contends that the specification does not show that the claimed composition would induce any anti-IL-15 antibodies in humans. Applicants respectfully disagree.

Firstly, Applicants have cancelled claims 1-13 and added new claims 14-22. The new claims are directed to compositions for generating neutralizing self-antibodies against autologous IL-15 and methods for treating IL-15 expression-related diseases by administering a composition comprising human IL-15, wherein the IL-15 is an antigen.

Applicants chose the simian model as proof of their concept to elicit self antibodies to a self protein because simian IL-15 has a 97% homology to human IL-15. In fact, there are changes in only 5 amino acids of the mature region of simian IL-15 as compared to human IL-15. Regarding their biological behavior, both simian and humans are identical. See Eisenman, et al., *Interleukin-15 Interactions With Interleukin-15 Receptor Complexes: Characterization and Species Specificity.* Cytokine, 2002, 20(3): 121-129.

As a result of their experiments with human IL-15 and simian IL-15, Applicants have observed recognition of peptides with sequences identical to simian IL-15, which suggests that "immunological tolerance" could be disrupted.

Applicants respectfully submit that a skilled artisan could easily make and use an IL-15 composition as described in the specification and administer the same to a human with the result being generation of neutralizing self-antibodies against autologous IL-15. Applicants ask the Examiner to reconsider the rejection under §112, first paragraph, in view of the new claims, declaration and above remarks.

With regards to claims 19 and 21 which recite the addition of a cytokine antagonist or anti-inflammatory drug, Applicants contend that cytokine antagonist and anti-inflammatory drugs are known to the skilled artisan.

With regards to the rejection of claim 12, Applicants have cancelled claim 12. Therefore the rejection of claim 12 has been rendered moot.

Rejections Under §112, Second Paragraph

Claims 1-13 have been rejected under §112, second paragraph as being indefinite. According to the Examiner, the IL-15 claimed is not defined by specific sequence identifier and thus the metes and bound of the term "IL-15" cannot be determined. The Examiner has interpreted "IL-15" as being full length human IL-15.

Applicants submit that the specification clearly intends that the "IL-15" claimed was obtained by a process using an E.coli recombinant clone. Therefore the obtained IL-15 has the same amino acid sequence as mature human IL-15, but a glycosylation pattern that is different from autologous IL-15. In particular, there is a disulphide bridge between Cys35 - Cys42 and between Cys85 - Cys88 in the IL-15 obtained using the E.coli recombinant clone. Native human IL-15 contains disulphide bridges between CYS35 - Cys85 and between Cys42 - Cys88.

Claims 6, 8 and 10 have been rejected for containing the phrase "such as." Claims 8-13 have been rejected for lacking steps. Claim 12 has been rejected for containing the phrase "like a DNA vaccine." In response, Applicants have cancelled the claims and added new claims that avoid the allegedly indefinite language.

Accordingly, Applicants respectfully request that the above rejections under §112, second paragraph, be reconsidered and withdrawn.

Rejections Under §102

Claims 1 and 2 have been rejected under §102(b) as being anticipated by U.S. Patent No. 6,013,480 to Grabstein et al. According to the Examiner, Grabstein et al.

disclose a vaccine composition comprised of yeast derived human IL-15 that stimulated production of anti-human IL-15 antibody producing cells in mice.

Claims 1 and 2 have been cancelled. New claims 14-22 claim compositions comprising IL-15 as an antigen for generating neutralizing self-antibodies against autologous IL-15. In claim 2, the IL-15 is a recombinant protein obtained in E. coli that has a glycosylation pattern different from autologous human IL-15.

Grabstein et al. do not disclose compositions comprising IL-15 as an antigen for generating neutralizing self-antibodies against autologous IL-15, or IL-15 as a recombinant protein obtained in E. coli that has a glycosylation pattern different from autologous IL-15. Therefore, Grabstein et al. do not anticipate the claims. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the §102(b) rejection based on Grabstein et al.

Claims 1, 2, 5-7, and 9-11 have been rejected as being anticipated by U.S. Patent No. 6,344,192 to Grooten et al. According to the Examiner, Grooten et al. disclose a pharmaceutical composition comprised of human IL-15.

Grooten et al. disclose use of human IL-15 as an adjuvant, and to promote CD4+ memory cells. Grooten et al. does not disclose using IL-15, according to the invention, to generate neutralizing self antibodies against autologous IL-15. Accordingly, the claimed

invention is not anticipated by Grooten et al. Applicants respectfully request that the Examiner reconsider and withdraw the §102 rejection based on Grooten et al.

Rejections Under §103

Claims 3-13 have been rejected under §103 as being unpatentable over of Grabstein et al. in view of Gonzalez et al.(Scand. J. Immunol. 2000, Vol.52, p. 113-116). Claims 3 and 4 (relating to IL-15 fused to p64k) have been cancelled.

According to the Examiner, Grabstein et al. disclose using human IL-15 to induce anti-IL-15 antibodies in mice, and therefore, it would have been obvious to use a vaccine composition comprising human IL-15 in methods of treating disease in mice. The Examiner also contends that Grabstein et al. disclose using cytokine antagonists.

Claims 1-13 have been cancelled and new claims 14-22 have been added. The new claims are directed at compositions comprising IL-15 as an antigen for generating neutralizing self-antibodies against autologous IL-15, and a composition where the IL-15 is a recombinant protein obtained in E. coli that has a glycosylation pattern different from autologous IL-15. Methods of using the compositions are also claimed.

In order to establish a prima facie case of obviousness, the cited documents, when combined, must disclose or suggest all of the claimed elements. Applicants have

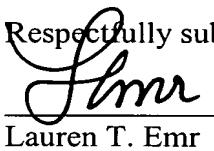
demonstrated the importance of the IL-15 being a recombinant protein obtained in E. coli that has a glycosylation pattern different from autologous IL-15.

Upon combining Grabstein et al. and Gonzalez, et al., the claimed invention is not disclosed or suggested. Therefore, the claimed invention is patentable over Grabstein et al. and Gonzalez et al.

Accordingly, Applicants respectfully request that the §103 rejection based on Grabstein et al. and Gonzalez et al. be reconsidered and withdrawn.

Applicants believe the application is now in condition for allowance. Should the Examiner feel that a telephone discussion with Applicants representative would be helpful in resolving any issues, he is invited to contact the undersigned at his convenience.

Respectfully submitted,



Lauren T. Emr
Attorney for Applicants
Reg. No. 46,139

HOFFMANN & BARON, LLP
6900 Jericho Turnpike
Syosset, New York 11791
(516) 822-3550
LTE:sbs
230380_1